65. (New) The humanized antibody of claim 35, wherein the specific immune response comprises production of HMFG-specific T cells.

66. (New) The fusion polypeptide of claim 34, wherein the immunoglobulin constant region is human.

67. (New) The fusion polypeptide of claim 34, wherein the immunoglobulin constant region is human.

68. (New) The immunogenic composition of claim 42, further comprising an adjuvant.

REMARKS

Telephone interview

Applicants' representative wishes to thank Examiner Burke for extending the courtesy of a telephone interview on July 14, 1999, and the helpful suggestions provided, which are reflected in this response.

Status of the claims; restriction; request for rejoinder

The Examiner has withdrawn the restriction between groups I and III. Thus, claims 1-5, 20-24, 26-37,[1] 39, 40, 42, 43, 54-56, and 59-61 are pending. By this amendment, claims 20-22, 26, 29, 30-32, 33, 35, and 39 have been amended, and new claims 62-68 added. Support for amendment the amendment of claim 20 is found in the specification, inter alia, on page 63, line 25 to page 64, line 7; page 64, lines 21 to page 65, line 8. Support for amendments to claim 26

[1] The Examiner states in the Office Action (page 2) that, inter alia, claims 26 and 35-37 are pending. However, in view of the withdrawal of the restriction between groups I and III, claims 27-34 (group III) are also pending and under consideration, as the Office Action Summary correctly indicates.

are in the specification on page 4, lines 15-20; page 5, lines 4-9; page 66, line 19 to page 67, line 13; Fig. 23. Support for amendments in claim 31 is in the specification ion page 69, lines 4-12 and Example 7. Claim 39 has been amended to be in independent format. Support for claims 66-67 is in the specification on page 71, lines 12-26 and Example 7. Support for claim 68 is on page 88, lines 15-16. Non-elected claims will be cancelled upon indication of allowable subject matter (i.e., in order to obtain a Notice of Allowance).

Applicants reiterate their request for rejoinder of presently excluded method claims, to the extent that they incorporate all the limitations of the product claims. The Examiner has indicated that once allowable product claims are identified, then method claims which incorporate all the limitations of the product claims and which do not present any new issues may be rejoined. Office Action, page 2. Applicants note that the Office's training document for rejoinder ("Training Materials for Treatment of Product and Process Claims in Light of *In re Brouwer* and *In re Ochiai* and 35 USC 103(b)", dated July 25, 1996) states that "[I]f applicant elects claims directed to the product, and the product is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product will be rejoined." Pages 3-4.

With respect to all claim amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Applicants acknowledge and appreciate withdrawal of the restriction between Groups I and III.

Compliance with sequence requirements

Applicants acknowledge and appreciate the Examiner's statement that the application is now in compliance with sequence requirements.

Amendment to the specification

As requested by the Examiner, the blanks on pages 14 (line 13) and page 78 (line 8) have been replaced with the appropriate serial number.

Rejections under 35 U.S.C. § 112, second paragraph

The following claims are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite: (a) 26; (b) 21-22 and 33; (c) 29-30; (d) 32; and (e) 35.

Claim 26. The Examiner states that the terms "homologous" and "HMFG" are indefinite. This claim has been amended to recite that at least two contiguous amino acids are homologous to a tandem repeat sequence from human mucin that is from HMFG. This human mucin is identified in the specification. See page 4, lines 15-20; page 5, lines 4-9; page 66, line 19 to page 67, line 13; Fig. 23. Further, mucin is known in the art. See Larocca et al. (1992) *Hybridoma* 11:191-201 (cited in the specification); Ceriani et al. (1983) *Somatic Cell Genetics* 9:415-427 (cited in the specification); and Gendler et al. (1990) *J. Biol. Chem.* 265:152886-15293. The term "homologous" has been deleted in the claim in favor of language that more precisely states that at least two contiguous amino acids of the polypeptide are identical to two contiguous amino acids in human mucin. See specification at page 66, line 26, to page 67, line 6.

Claims 21-22 and 33. These claims have been amended to refer to the light or heavy chains of 11D10 (by use of the word "the").

Claims 29-30. The terms "GM-CSF" and "IL-2" have been spelled out, although Applicants respectfully submit that the meaning of these abbreviations is well-understood by those skilled in the art.

Claim 32. This claim has been amended to refer to the contiguous amino acids from SEQ ID NOS: 2 and 4 which are recited in claim 31.

Claim 35. Claim 35 is rejected as allegedly indefinite for reciting "humanized antibody". This claim has been amended to recite that the humanized antibody contains three CDRs from

the light chain variable region of 11D10 and three CDRs from the heavy chain variable region of 11D10 and that the humanized antibody is able to stimulate a specific immune response against HMFG. The concerns expressed by the Examiner should be addressed by these limitations.

In view of the discussion above, Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph be withdrawn.

Deposit of biological materials

The Examiner has suggested depositing the hybridoma that produces 11D10 for enablement purposes. This deposit was disclosed in the specification on page 14, lines 6-10. The Examiner indicates that the previously submitted, unsigned declaration of Malaya Chatterjee would be persuasive if it were signed. Attached to this response is the signed declaration with a copy of the deposit receipt.[2] Applicants note that the Examiner stated that the declaration submitted and signed by Applicants' representative was not persuasive without providing any reasons why the this declaration was not satisfactory.

Applicants also respectfully note that the deposit information should not be a basis of a rejection under 35 U.S.C. § 112, first paragraph; nor had this been indicated prior to the present Office Action. The Examiner states that "it would require undue experimentation to reproduce the claimed antibody species 11D10". Office Action, page 7. Applicants respectfully disagree. The amino acid sequence of the variable regions of 11D10 are provided in the specification, which also discloses methods to produce 11D10. See page 34, line 20, to page 36, line 18.

Applicants respectfully request that the Office acknowledge for the record that the deposit information is complete and that, to the extent there are any rejections based on alleged lack of deposit information, they be withdrawn.

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[2] Applicants also note that, according to the Office Action, the declaration was not required, because the deposit was made before the effective filing date of the application.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 20-24, 26, 35-36, 39, 42, 61 and 56 are rejected under 35 U.S.C. § 112, first paragraph as allegedly non-enabled. Specifically, the Examiner states that the specification is enabling for polypeptides which contain all six CDRs of 11D10.

In the interest of expediting prosecution, Applicants have amended the claims to recite that the claimed polypeptide must have three CDRs from the light or heavy variable regions of 11D10. Applicants also note the following.

The Examiner points to a statement by Chatterjee et al. that "the art-recognized experience that for any novel therapy, the transition for the laboratory to the clinic. . . is a quantum leap". Office Action, page 8. The Examiner also states that "few examples have appeared in the application of autoimmune antibodies as part of immunotherapy to human tumors, it is not clear from the specification whether autoantibodies can generate antitumor responses to all tumors, in all species, and to what degree". Office Action, pages 8-9. Applicants do not understand these references to therapy. The claims recite that the polypeptide(s) has the immunological activity of an ability to stimulate a specific immune response against human milk fat globule (HMFG).

The Examiner also discusses this rejection in terms of the requirement for formation of an antigen-binding site, and that [ò]ne skilled in the art would reasonably expect that in order to generate an anti-HMFG response, that all six CDRs of the anti-idiotypic antibody are necessary". Office Action, pages 9-10. The claims recite that the polypeptide(s) be able to stimulate a specific immune response to HMFG. The requirements for immunostimulation by a peptide are less stringent than those for binding of antigen to antibody. As is well known in the art, peptides as small as 5 amino acids in length can be immunogenic. An immunostimulatory peptide from an anti-idiotype antibody would be effective if it had sufficient determinants to be immunostimulatory and sufficient similarity with target antigen so that the response would have the desired specificity.

The Examiner's attention is also directed to U.S. Ser. No. 08/591,196, which has been allowed by the Office, under examination by the Examiner. Based on virtually identical facts, the Office allowed claims which recite that the polypeptide comprises three light chain CDRs or three heavy chain CDRs from the anti-idiotype antibody, based on disclosure of an anti-idiotype antibody sequences.

The Examiner states that "[t]he specification provides no direction or guidance regarding how to produce fusion proteins and antibodies as broadly defined by the claims". Office Action, page 10. The specification describes making fusion proteins (methods of which are known in the art) on page 68, lines 12, to page 70, line 25; Example 6. The range of 11D10 amino acid sequences which may be included in a fusion protein comprising an 11D10 polypeptide are described in the specification on page 63, line 25, to page 67, line 13.

With respect to the Examiner's statements regarding humanized antibodies (known in the art and disclosed in the specification on page 71, lines 12-26), Applicants note that the claim directed to a humanized antibody, claim 35, has been amended to recite that this antibody contains all six CDRs.

Applicants respectfully request that this rejection be withdrawn.

Rejections under 35 U.S.C. § 102

102(b)

Claims 1-5, 20-27, 31-33, 36, 37, 39, 40, 42, 43, 55, 56, and 59-61 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by any of the four references listed in the Office Action on page 11. The Examiner states that "[c]learly 11D10 has been described in written publications more than a year before the filing of the U.S. application", and states that the unsigned declaration addresses only the lack of public availability of 11D10.

The previous response dated October 8, 1998, discussed in detail why no reference anticipates the invention, primarily because none of these references is enabling. In summary,

none of the cited publications anticipates the pending claims because (a) the cited references are not enabling because they do not teach an/or enable obtaining 11D10 antibody, and do not disclose the amino acid sequence or DNA coding sequence for the variable regions of 11D10, and thus cannot be used as a prior art reference; and (b) neither 11D10 nor the hybridoma producing 11D10 were made available to the public. With respect to the references being non-enabling, the previous response (dated October 8, 1998), discussed in detail the mechanism of antibody formation as well as the uniqueness of the 11D10 sequence (which was not disclosed in any of the references).

The Examiner makes no reference to these arguments that are on the record. Moreover, Applicants respectfully point out that the Examiner has already considered virtually identical facts and arguments in two other related cases, one of which has matured into an issued U.S. patent (5,612,030), and the other allowed (U.S. Ser. No. 08/579,940). Applicants respectfully submit that ample reasons have been provided as to why none of the cited references anticipates the invention, and request that this rejection be withdrawn.

With respect to the declarations of Drs. Malaya Chatterjee, Sunil Chatterjee, and Kenneth Foon, addressing lack of public availability of 11D10, accompanying this response are the signed declarations. These declarations were discussed in the previous response.

Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be withdrawn.

102(f)

Claims 1-5, 20-27, 31-33, 36-37, 39, 40, 42, 43, 55, 56 and 59-61 are rejected under 35 U.S.C. § 102(f) by the references cited by the Examiner in the Office Action on page 13. The Examiner has considered the unsigned declaration of Malaya Chatterjee[3] and states that the declaration is persuasive with respect to Ceriani, Kohler and Sherratt. However, the Examiner is

[3] The Examiner refers to also considering the declarations of Drs. S. Chatterjee and K. Foon; however, only Dr. Malaya Chatterjee's declaration addresses the inventorship issue.

still unconvinced with respect to Drs. Mrozek, Mukerjee, and Chakraborty for the following reasons: (a) the declaration fails to state whatever scientific contribution Dr. Chatterjee may have made in the production and characterization of 11D10 antibody and hybridoma; (b) the declaration states that the hybridoma which produces 11D10 was generated by Dr. Mrozek and that the 11D10 antibody was generated and characterized by Drs. Mukerjee and Chakraborty; and (c) the declaration is unsigned.

With respect to reason (a), Dr. Chatterjee's declaration states that she chose the protocols and criteria to be followed for developing and selecting the 11D10 antibody; that she instructed Drs. Mrozek and Mukerjee to follow these protocols; that they reported the results of their experiments to her; and that she chose 11D10 as the most desirable antibody.

With respect to reason (b), Dr. Chatterjee's declaration states that Drs. Mrozek, Mukerjee and Chakraborty did not make any independent contributions to generating 11D10 or the 11D10 producing cell line. They were all working under Dr. Chatterjee's direct supervision.

With respect to reason (c), accompanying this response is the signed declaration, which should remove this ground for rejection. The information in Dr. Chatterjee's declaration should be sufficient to overcome the rejection, and during the telephone interview the Examiner indicated that this information would be sufficient.

In view of the above, Applicants respectfully request that the rejection under 35 U.S.C. § 102(f) be withdrawn.

102(e)

Claims 20, 22, 24, 26, 33-36, 39, 42, 56 and 61 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Gourlie et al. (U.S. Pat. 5,808,033) and Bendig et al. (U.S. Pat. 5,840,299). The Examiner states that the sequence VRSGA disclosed in Gourlie et al. consists of CDR1 of SEQ ID NO:4 (heavy chain), and the sequence MTQSPSSLSAS disclosed in Bendig et al. are sequences of CDR1 of the 11D10 light chain, as depicted in SEQ ID NO:2.

Applicants respectfully point out that neither of these sequences discloses a CDR as recited in the claims. The CDRs are depicted in Figure 3. The SEQ ID NOs referred to by the Examiner contain the entire variable regions. As shown in Figure 3B, the sequence VRSGA is in framework #1; as shown in Figure 3A, the sequence MTQSPSSLSAS is in framework #1.

Further, Applicants note that claim 20 has been amended to recite that the claimed polypeptide contains three CDRs.

Applicants request that rejections under 35 U.S.C. § 102(e) be withdrawn.

Publication policy

The following publication policy of the journal of *Cancer Research* has come to the attention of Applicants' representative:

"It is understood that by publishing any work in *Cancer Research* the authors agree to make freely available to other academic researchers any of the cells, clones of cells or DNA or antibodies, etc. that were used in the research reported and that are not available from commercial suppliers. Also, authors may be required to make primary data available to the Editor-in-Chief in cases of dispute."

CONCLUSION

Applicants believe they have addressed all issues raised by the Office and that the claims are in condition for allowance, which is respectfully requested. If the Examiner wishes to discuss this application or provide comments, she is invited to telephone Applicants' representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 30414-2000321. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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